Three Examples of Chordoma

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CHORDOMATA, or tumours derived from remnants of the notochord, are not common, the first recognized example in this country having been described by Stewart as recently as 1922. The tumours are usually slowly growing and possess a comparatively low grade of malignancy, but their surgical extirpation is extremely difficult, if not impossible. Further, one of their favourite sites of origin is in the base of the skull—at or near the spheno-occipital synchondrosis—so that a timely recognition of the nature of the growth might spare the patient one or more major operations and the surgeon a hopeless task. Chordomata of the sacral region, and of other parts of the vertebral column, are more accessible to surgery; therefore the prognosis is not quite so unsatisfactory as in the cranial growths, but even here it is not good.

Of the three examples recorded in this paper one (Case I) was discovered at post-mortem examination growing from the region of the spheno-occipital synchondrosis. The site of origin of the other two is doubtful, because both are biopsy specimens, one (Case II) from the neck, and the other (Case III) from the retropharynx.

Small localized proliferations of notochordal tissue were recorded by Luschka and Virchow (1857-8), growing in the form of soft, jelly-like masses from the region of the clivus and penetrating the dura mater. Virchow regarded them as ecchondroses, but they were peculiar in that they contained large vacuolated cells, perhaps arising from degeneration. He introduced the term "ecchondrosis physaliphora" to describe them. Soon afterwards Müller suggested, on the basis of comparative anatomical studies, that these formations were derived from notochordal remnants, and his opinion was ultimately confirmed by Ribbert (1894). Their notochordal origin is now generally accepted, and the term "eccordosis physaliphora spheno-occipitalis" was introduced by Stewart, who observed four of them in a special series of 350 consecutive autopsies. Larger masses of a fundamentally similar nature, but possessing the property of slowly progressive growth and showing a tendency to recur after removal, may arise in the clivus and in other situations in the spinal column, and it is to this type of tumour that the term "chordoma" is applied. Stewart (1922) presents an historical summary together with a list of cases published prior to that time. Stewart and Morin (1926) publish a review of the literature and record a new case. Cappell (1928) indicates an interesting parallel between the developing notochord in the dogfish and the evolution of the fully formed tumour.

It will be recollected that in the human subject the notochord disappears comparatively early in the life of the embryo, and persists only as the nucleus pulposus in the intervertebral discs. It has been shown, however, that in addition to the ecchordosis physaliphora spheno-occipitalis described above, small remnants may be found on occasion almost anywhere in the spinal column. It is conceivable that

from such elements tumour formations arise. Theoretically, then, one might anticipate the appearance of chordoma in any situation in or near the confines of the original notochord, but in actual practice the tumour is found with much greater frequency in positions corresponding to the upper and lower extremities of this structure. Stewart and Morin (1926) point out that in a series of fifty-five tumours twenty-five occur in the region of the spheno-occipital synchondrosis and twenty-seven in the sacro-coccygeal region. Examples of the tumour in other situations are not wanting, however, as evidenced by those of Cappell (1928) in the cervical and dorsal region, Hutton and Young (1929) in the dorsal region, and Davison and Weil (1928) in the lumbar region.

NAKED-EYE APPEARANCES OF CHORDOMA.—The macroscopic appearances are highly characteristic, the tumour presenting itself as an encapsuled and lobulated growth. The inter-lobular septa are composed of fibrous tissue, and the spaces are occupied by whitish semi-transparent material of a gelatinous nature. The degree of malignancy is apparently inversely proportional to the amount of this gelatinous substances present for the active varieties present a solid opaque appearance. The whole formation bears some resemblance to the "mixed parotid tumour," or in some cases to a "mucoid" carcinoma. The tumours vary greatly in size and may on occasion attain very large dimensions. A spheno-occipital growth measuring eleven centimetres in length is described by Jelliffe and Larkin (1912), whilst that of Willis (1930) occurring in the sacro-coccygeal region was fifteen inches in length.

Chordoma usually is slow-growing and of low malignancy, but it tends to recur after removal. A particularly notable feature is its tendency to destroy adjacent bone. In the intracranial cases, penetration of the skull with extension into the nasopharynx, orbits, and sinuses is not uncommon. The tumour may also grow upwards into the interpeducular region, as in the case described by Bailey and Bagdasar (1929). In the sacro-coccygeal region, invasion of sacrum, coccyx, and os innominatum, with ulceration into the rectum, has been described. A notable feature of this group is the manner in which the skin remains intact even when stretched over a very large tumour mass. In the cervical region, extension into the nasopharynx, fauces, and laryngopharynx occurs.

Metastases would appear to be relatively uncommon, although these have been described in the cervical glands by Lewis (1921) and over the right scapula by Stewart (1922). In Willis's sacro-coccygeal case (1930), very widespread metastases occurred in lung, spleen, liver, kidney, etc., this being attributed to direct spread by the iliac veins.

HISTOLOGICAL APPEARANCE.—Microscopically the tumour comprises a dense fibrous stroma, part of which goes to form the capsule and part of which is involved in the production of the interlobular trabeculæ. Resting on this fibrous tissue there are columns and solid alveolar masses of epithelial cells. The younger or more recent areas are composed of solid aggregates of epithelial cells with uniformly staining cytoplasm, but later these cells are liable to become vacuolated. Later still, this vaculation is very marked, producing the so-called physaliphorous cells. Occasionally individual cellular outlines are lost, resulting in the production

of masses of vacuolated syncytium. The vacuoles would appear to be due to the production within the cells of mucin, and this passes out into the intercellular spaces, where it tends to lie in columns. Ultimately, what may be described as a pool of mucin is formed in which only a few isolated islands of cells remain This pool is surrounded by tumour cells, and it may contain extravasated blood.

The cells themselves vary greatly in shape and size, mitotic figures are not uncommon, and there is reason to believe that amitotic division, which is said to occur in the primitive notochord, also takes place in the chordoma. Nuclear hyperchromatism is a prominent feature. Nuclear vacuolation was emphasized by Stewart (1922) and Cappell (1928), but the nature of the contents of these vacuoles is not known. Another interesting feature is the presence of glycogen within the cells, especially the actively growing ones.This is apparently independent of the mucinous secretion, and no support can be lent to the suggestion that the nuclear vacuoles contain this substance.

Clinical Aspects.—Age does not appear to play a very important part in the incidence of the tumour, but the majority of cases occur between the ages of 30 and 50 years. The growth has been recorded, however, in patients of 16 and 68 years. Males are affected rather more often than females.

The symptoms of the spheno-occipital group are those of any other slowly-growing tumour at the base of the brain. Headache, vomiting, and papillœdema are frequent symptoms, and appear at a comparatively early stage. As the growth increases in size, involvement of various cranial nerves is manifest. Symptoms of bulbar paralysis may ensue, or, again, the signs may point to a tumour of the cerebello-pontine angle. Epileptiform seizures have been described (Stanton, 1932).

The prognosis in this group is very unfavourable, the average duration of life after the first appearance of symptoms being two years. Operative interference can only meet with partial success, owing to the fact that the tumour invades and destroys the base of the skull. In one case, described by Bailey and Bagdasar (1929), a tumour of the suprasellar region was removed by currettage and the patient was in good health fifteen months later, but this would seem to be rather exceptional.

In the sacro-coccygeal region, the tumour presents itself as a slowly-growing, firm, elastic mass situated in the middle line. Symptoms depend upon whether the growth extends inwards towards the rectum, or tends to spread posteriorly to appear beneath the skin of the back. Pain in the coccyx is usual in either event. Tumours situated anteriorly may be palpated through the rectum, and pain and difficulty in defæcation, sometimes accompanied by blood-stained mucus in the stools, will be noted. Where the growth is posterior to the sacrum its presence beneath the skin should lead to a provisional diagnosis of chordoma. Treatment consists in wide surgical removal at the earliest possible opportunity. A portion of normal bone should be removed together with the tumour. It would seem that recurrence takes place in the vast majority of cases, but sometimes the secondary growths can be removed with success. Owing to the slow nature of the growth recurrence may not take place for many years, and relief from symptoms for long periods is recorded. Radium and deep X-ray therapy appear to be of little value.

Case I.

A male patient, aged 33, whose previous health had been good, first came under observation on 21st November, 1931. He gave a history of increasing hoarseness for a period of six months prior to this date. Three months previously he had commenced to suffer from dysphagia. He noticed that phlegm tended to gather in his throat.

On examination his general condition was good. His sight, fields of vision, and fundi, were normal. No abnormality of the third, fourth, fifth, sixth, seventh, and eighth cranial nerves was detected. The palate was drawn up and deviated to the right. The tongue deviated to the left on protrusion. The left vocal chord was immobile. There was dropping of the left shoulder associated with wasting of the trapezius and sterno-mastoid muscles of that side. The Wassermann reaction was negative, and C.S.F. and X-ray examination yielded nothing of note.

This patient next came under observation on 18th October, 1932. He was then suffering from severe headache, generally frontal in situation, but occasionally occipital. He complained that his vision was dim and that he staggered when he walked. He vomited occasionally in the morning.

On examination the general condition was fair. The left optic disc was blurred in outline, the right normal. The pupils were unequal (left 4 mm., right 3 mm.). The left was inactive to light. The consensual reflex was present on both sides, but diminished on the left. The reaction to accommodation was greater on the right than on the left. Lateral nystagmus to either side was present. The fifth, seventh, and eighth cranial nerves were normal. The tongue was markedly atrophic on the left side, and on protrusion deviation to that side occurred. The palate was raised in the middle line. The voice was normal. Weakness was present in the left deltoid and trapezius muscles. The left sterno-mastoid appeared to have recovered. Dorsiflexion of the great toe occurred on the left side on attempting to elicit the plantar reflex. The response on the right side was normal. The gait was slightly reeling in character, with a tendency to deviate to the right. Romberg's sign was absent.

On 13th November, 1932, the base of the brain was exposed at operation. A tense, firm, encapsulated tumour was observed between the spinal cord and the foramen magnum. It was pressing on the left hypoglossal nerve. No attempt at removal was made, and the patient died next day.

The post-mortem examination was performed by Professor Young. A brief résumé of the salient facts is given :—

The dura mater and the cerebral hemispheres were normal in appearance. The cerebrum was removed by section of the peduncles in order to expose the posterior fossa without disturbance of the anatomical relationship. At this stage a rounded extradural tumour was observed on the surface of the basi-sphenoid to the left of the middle line. The cranial nerves eight, nine, ten, and eleven, were stretched over the surface of the growth on the left side, but they were not directly involved and could be readily detached. The spinal cord was then exposed, and was removed intact in continuity with the medulla, cerebellum, and brain stem. The tumour was now completely exposed. It was elongated from before backwards, and apparently extradural in its whole extent. It measured two inches by one inch. The base of the skull was removed with the tumour intact.

Case II.

A male patient, aged 26, was first examined on 23rd November, 1933. He stated that he had had a slowly growing swelling in the left side of his neck for seven months. This caused pain and limitation of movement on chewing. There was no dysphagia. His throat was occasionally painful.

On examination a swelling about the size of a tangerine orange was found below the left ear. It was firm, smooth, and painless. A smaller similar swelling was observed below the right ear. The left tonsil was rough, and there was proptosis of the left eye. The pupils were unequal and slightly irregular. They reacted sluggishly to light and accommodation. X-ray of the skull yielded no definite information.

On 1st December, 1933, a portion of the tumour was removed for microscopic examination. On 14th December, 1933, deep X-ray therapy was commenced, and the patient was discharged two days later with instructions to return at stated intervals for further X-ray treatment.

Case III.

A male patient, aged 60, was first seen on 16th January, 1934. Three years previously he had experienced difficulty in breathing through his nose. Eighteen months later he underwent an operation on his left nostril. He was unable to state the nature of this operation, and no record was available. He stated that for some time afterwards his breathing was improved, but gradually it reverted to its original state.

On examination he was only able to breathe through his mouth, and also suffered from some degree of dysphagia. The soft palate was displaced forwards by a mass about the size of an egg situated beneath the mucous membrane of the posterior pharyngeal wall. The mass was firm and painless, and the mucosa overlying it free from ulceration. X-ray confirmed the clinical diagnosis of retropharyngeal tumour.

At operation on 20th January, 1934, the soft palate was divided with the diathermy knife and the mass exposed. It was incised in the midde line vertically, and the contents removed piecemeal. The cavity was cleaned and the palate sutured. The patient was discharged from hospital five weeks later.

Comment.—Microscopically the three tumours present the characters of chordomata as tabulated above.

Case I represents an intracranial growth occurring in a typical situation, and producing the symptoms of increased intracranial pressure together with involvement of certain of the cranial nerves. The progress and duration of the case are such as might be expected from the previous records.

The site of origin of the growth in Case II is a matter for considerable speculation. Three possible theories might be advanced :—

(*a*) That the primary focus is in the spheno-occipital region, and direct extension into the neck has occurred.

(*b*) That a similar extension has taken place from a tumour originating in one of the cervical vertebræ.

(*c*) That the mass in the neck represents secondary glandular involvement from a tumour in either site. No glandular structure was, however, observed in the microscopic preparations.

In Case III it is reasonable to assume that the growth has originated in the basisphenoid region, and extends directly behind the posterior pharyngeal wall.

The histological appearances in all three cases leave little room for doubt, although Ewing (1928) issues a note of warning against the possibility of confusion of this type of tumour with myxochondroma or "colloid" carcinoma. The microscopic picture in each case was, however, highly characteristic.

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An Anencephalic Embryo of 25 mm. C.R. Length

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ONE of the commonest malformations of the human fœtus is anencephalus. Descriptions have been given of it since earliest times, but the first worker to give a clear account of it as "an arrested closure of the primitive neural groove" was von Recklinghausen[1] in 1886. Since this time his description has been accepted by all writers, and Faldino[2] in more recent times has confirmed his work. This description, however, makes no attempt to discuss the factors which inhibit the closure of the medullary groove, and many writers since von Recklinghausen have made tentative studies to discover the basic influence. Gaddi[3] claimed that a constant feature was the absence or aplasia of the supra-renal body, a claim substantiated by other writers. Mandruzzatio,[4] in a long description of an anencephalic human embryo of 48 mm. length "from vertex to the podalic extremity," states that there were present "noticeably hyperplastic supra-renal glands," the converse condition from that found by Gaddi. The other ductless glands were not discussed.

With this divergence of opinion on the subject of the condition of the supra-renals, and without any observations on the other glands, the appearance of a human anencephalic embryo of 25 mm. C.R. length in my laboratory was hailed as an opportunity to study, in this malformation, the condition of the supra-renal and other ductless glands, and to learn if support could be found for either of the views expressed by the many writers on the subject. It must be remembered that the development of this embryo is greater than its total length would at first suggest, owing to the absence of head development. If the head had been of normal size, the total C.R. length of the embryo would have been increased by about 10 mm. The stage of development of the structures of the embryo, apart from the abnormal regions, also suggest that it should be compared to an embryo of 35 mm., and as a consequence I have adapted this standard for purposes of comparison.

The embryo was first photographed (figs. 1 and 2), and then cut into transverse sections of ten microns thickness. The sections were then stained in alternate slides with hæmatoxylin and eosin, and with Mallory's triple connective tissue stain. These sections showed the supra-renal glands to be normal in development and differentiation for an embryo of 35 mm. C.R. length.* They also showed the

* In a full-term human anencephalic fœtus which I was enabled to study, marked hypoplasia of both supra-renal glands was observed. This condition agrees with the description given of all full-term anencephalics in the literature. It would seem, therefore, that taken in conjunction with